

REMARKS

Claims 6, 10-11, 17, 20, 22, 27-29, 31-35, and 37 are pending in the subject application. Claims 1-5, 7-9, 12-16, 18-19, 21, 23-26, 30 and 36 have been canceled. Claims 27-28, 32, 34, 35 and 37 have been amended. No new matter is raised by these claims amendments.

It appears that the Examiner did not address amendments made to claims 6, 17, 27 and 28 in the Amendment filed on February 17, 2004. In the office action dated February 27, 2004, the Examiner stated that "Gonzales teaches a method. . . (c) amplifying the mRNA with primers which are *substantially identical* to SEQ ID NO: 1 and 2." (Emphasis added). Yet claims 6-11, 17-22, 26, 27-35 and 37 have been amended such that the language "substantially identical" is irrelevant. The Examiner did not address these claims in the office action as they were previously amended. Rather, the Examiner continues to reject these claims in their previous arrangement.

Rejection under 35 U.S.C. § 103(a)

Claims 6-11, 17-22, 27-29, 31-35 and 37 have been rejected under 35 U.S.C. § 103 (a) over Gonzalez et al. (U.S. Patent 6,015,673) in view of Willhauck et al. (Biotechniques (1998) 25:656-659) and further in view of Stanta et al. (Biotechniques (1991) 11(3): 303, 306, and 308).

Applicants respectfully disagree as Gonzalez does not teach each and every element of the claimed invention and Willhauck and Stanta do not make up for these deficiencies. The fact that Gonzalez teaches a method of freezing or fixing a sample for detection is irrelevant, as the present claims involve fixing a portion of a tumor sample in paraffin. Gonzalez does not teach or suggest this. The present claims involve isolating mRNA from the fixed and paraffin embedded (FPE) tumor tissue. Gonzalez does not teach or suggest this. The present claims involve amplifying mRNA from the FPE tumor tissue. Gonzalez does not teach or suggest this. The present claims also involve comparing expression levels of DPD in the amplified mRNA from the FPE tumor sample with the mRNA from an

internal control gene. Gonzalez does not teach or suggest this. Willhauck does not teach or suggest these missing elements and does not make up for the shortcomings of Gonzalez. For example, the Examiner cites Willhauck for teaching comparing the amount of the target gene to an internal gene including B-actin. Willhauck, however, actually teaches away from the use of housekeeping genes, such as GAPDH and B-actin. (See page 656 column 1). Specifically, Willhauck states that such housekeeping genes are “not suitable for reliable detection of tumor targets with low mRNA expression levels.” Thus, applicants respectfully assert that the combination of Gonzalez and Willhauck does not teach nor suggest the claimed invention and therefore does not render the claims obvious.

In response to the Examiner’s assertion that it would be obvious to one skilled in the art to combine the teaching of Gonzalez with Willhauck and Stanta, as addressed above, the applications respectfully disagree. Applicants argue that as with Willhauck, Stanta actually teaches away from the claimed invention and, thus, one would not be motivated to combine the teachings of Gonzalez with the teachings of Stanta to arrive at the presently claimed invention. For example, the Examiner cites Stanta for teaching a chaotropic agent, yet Stanta, on page 307 column 1, characterizes the second step of the method as teaching “a proteolysis step with a high concentration of proteinase K in the presence of 1 M guanidinium thiocyanate” to allow for efficient RNA extraction without further degradation. In contrast, the claimed method uses a chaotropic agent (without a high concentration of proteinase K) at higher temperatures for shorter times to extract mRNA from fixed paraffin embedded samples. Further, unlike the asertion that “six hours” is “about” 120 minutes is nonsensical. Additionally, in light of the present amendments, the allegation that 45° C was “about 50 to about 120 °C” or “about 75 to about 120 °C” and that 6 hours is “about 120 minutes” is now moot. Thus, applicants respectfully assert that the combination of Gonzalez and Stanta does not teach nor suggest the claimed invention and therefore does not render the claims obvious. Accordingly, applicants respectfully request withdrawal of this ground of rejection.

Applic. No. 09/842,111
Amdt. dated May 26, 2004
Reply to Office Action of Feb. 27, 2004

CONCLUSION

It is believed that the present claims are in conditions for allowance and earnestly request allowance. Extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 11-0600. The Examiner is invited to contact the undersigned attorney if necessary to expedite allowance.

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Respectfully submitted,

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